CLAIMS

What is claimed is:

1. A method for identifying an agent that inhibits the catalytic activity of PTPbr7, comprising the steps of:

(a) combining, in a first cocktail, an amount of a PTPbr7, an amount of a substrate capable of being dephosphorylated by PTPbr7, and an amount of a test agent, in an assay buffer comprising a reducing agent;

(b) preparing a second cocktail comprising all of the ingredients of said first cocktail except for said test agent;

(c) incubating said first and second cocktails under conditions suitable to allow for a substantial amount of dephosphorylation of said substrate by said PTPbr7;

(d) terminating said incubation;

(e) quantitating the amount of dephosphorylation in each of said cocktails; and

(f) comparing said amounts of dephosphorylation;

where a PTPbr7 inhibitor is a test agent whose presence results in less dephosphorylation than its absence.

2. The method as defined in claim **1** wherein said PTPbr7 is full length.

3. The method as defined in claim **2** wherein said PTPbr7 is recombinant rodent PTPbr7.

4. The method as defined in claim **3** wherein said rodent is a mouse or a rat.

5. The method as defined in claim **1** wherein said PTPbr7 is a fusion protein comprising the catalytic domain of PTPbr7 and a heterologous sequence.

6. The method as defined in claim **5** wherein said PTPbr7 is fused N-terminally to said heterologous sequence.

7. The method as defined in claim **5** wherein said PTPbr7 is fused C-terminally to said heterologous sequence.

8. The method as defined in claim **5** wherein said heterologous sequence is glutathione-S-transferase or a six-histidine residue tag.

9. The method as defined in claim **1** wherein said substrate is a small molecule mimetic.

10. The method as defined in claim **9** wherein said small molecule mimetic is para-nitrophenylphosphate.

11. The method as defined in claim **1** wherein said terminating is by adding a base to said assay buffer.

12. The method as defined in claim **11** wherein said base has a final concentration in said assay buffer of 0.95N NaOH.

13. The method as defined in claim **1** wherein said substrate is para-nitrophenylphosphate, a phosphoprotein, or a peptide having a phosphotyrosine residue.

14. The method as defined in claim **1** wherein said substrate is a phosphoprotein, or a peptide having a phosphotyrosine residue.

15. The method as defined in claim **14** wherein said peptide is [ENDpYINASL] or [DHTGFLTEpYVATRW].

16. The method as defined in claim **14** wherein said phosphoprotein is MAPK-P.

17. The method as defined in claim **1** wherein said suitable conditions for dephosphorylation are a temperature of from about room temperature to about 37°C, and an incubation time of from about 5 min to about 90 min.

18. The method as defined in claim **1** wherein said assay buffer comprises a buffer, a salt, and a detergent.

19. The method as defined in claim **18** wherein said buffer is Tris or Hepes, said salt is NaCl, and said detergent is Tween-20.

20. The method as defined in claim **19** wherein said buffer is 50 mM Tris or 50 mM Hepes, said salt is 150 mM NaCl, and said detergent is 0.05% Tween-20.

21. The method as defined in claim **1** wherein said reducing agent is DTT or BME.

22. The method as defined in claim **14** wherein said amount of said assay buffer is about 25 μL, said assay buffer comprises about 50 mM Tris, about 0.15 M NaCl, about 5 mM DTT, and about 0.1% BSA, at about pH 7.4, said terminating is by adding a stop solution comprising malachite green dye, ammonium molybdate, and

Tween-20 to said cocktails, and waiting about 15 min, and said quantitating is by measuring the optical density at 620 nm of each of said stopped cocktails using a spectrophotometer, and comparing the optical density values with a set of standards comprising varied amounts of inorganic phosphate in said stop solution.

23. A pharmaceutical composition comprising an inhibitor of the catalytic activity of PTPbr7 as defined in claim **1** and a pharmaceutically acceptable carrier, vehicle, or diluent.

24. A method for treating a condition or disease in a mammal comprising administering to said mammal a pharmaceutical composition as defined in claim **23**.

25. A method for identifying an agent that inhibits the catalytic activity of PTPbr7, comprising the steps of:

(a) combining, in a first cocktail, an amount of a PTPbr7, an amount of a substrate capable of being dephosphorylated by PTPbr7, and an amount of a test agent, in an assay buffer comprising a reducing agent;

(b) preparing a second cocktail comprising all of the ingredients of said first cocktail except for said test agent;

(c) incubating said first and second cocktails under conditions suitable to allow for a substantial amount of dephosphorylation of said substrate by said PTPbr7;

(d) quantitating the amount of dephosphorylation in each of said cocktails; and

(e) comparing said amounts of dephosphorylation;

where a PTPbr7 inhibitor is a test agent whose presence results in less dephosphorylation than its absence.

26. The method as defined in claim **25** wherein said PTPbr7 is full length.

27. The method as defined in claim **25** wherein said PTPbr7 is recombinant rodent PTPbr7.

28. The method as defined in claim **27** wherein said rodent is a mouse or a rat.

29. The method as defined in claim **25** wherein said PTPbr7 is a fusion protein comprising the catalytic domain of PTPbr7 and a heterologous sequence.

30. The method as defined in claim **29** wherein said PTPbr7 is fused N-terminally to said heterologous sequence.

31. The method as defined in claim **29** wherein said PTPbr7 is fused C-terminally to said heterologous sequence.

32. The method as defined in claim **29** wherein said heterologous sequence is glutathione-S-transferase or a six-histidine residue tag.

33. The method as defined in claim **25** wherein said substrate is a small molecule mimetic.

34. The method as defined in claim **33** wherein said small molecule mimetic is O-methylfluorophosphate.

35. The method defined in claim **34** wherein said quantitating is by measuring the excitation at 485 nm and fluorescent emission at 535 nm of each of said cocktails using a fluorometer.

36. The method as defined in claim **25** wherein said suitable conditions for dephosphorylation are a temperature of from about room temperature to about 37°C, and an incubation time of from about 5 min to about 90 min.

37. A pharmaceutical composition comprising an inhibitor of the catalytic activity of PTPbr7 as defined in claim **25** and a pharmaceutically acceptable carrier, vehicle, or diluent.

38. A method for treating a condition or disease in a mammal comprising administering to said mammal a pharmaceutical composition as defined in claim **37**.

39. A method of screening for an agent that inhibits the catalytic activity of PTPbr7, comprising the steps of: exposing cells or a cell line expressing PTPbr7 and capable of responding to NGF, to an amount of NGF, in the presence and absence of a test agent, under conditions suitable for a detectable NGF response to occur in the presence of a PTPbr7 inhibitor, detecting said response, and comparing said response, where a PTPbr7 inhibitor is a test agent whose presence results in more of an NGF response than its absence.

40. The method as defined in claim **39** wherein said cell line is a PC12 cell line, or a PC12 cell line stably transfected with a PTPbr7, and said cells are primary neurons, or primary neurons cotransfected with a cDNA clone of a PTPbr7 and lac Z.

41. The method as defined in claim **40** wherein said primary neurons are cholinergic neurons.

42. The method as defined in claim **41** wherein said cholinergic neurons are basal forebrain neurons.

43. The method as defined in claim **40** wherein said transfected PC12 cell line overexpresses said PTPbr7, and said primary neurons overexpress said PTPbr7.

44. The method as defined in claim **40** wherein said NGF response is neurite outgrowth.

45. The method as defined in claim **39** wherein said NGF response is survival.

46. The method as defined in claim **39** wherein said NGF response is the expression of any gene induced by NGF.

47. The method as defined in claim **39** wherein said NGF response is MAPK phosphorylation.

48. A pharmaceutical composition comprising an inhibitor of the catalytic activity of PTPbr7 as defined in claim **39** and a pharmaceutically acceptable carrier, vehicle, or diluent.

49. A method for treating a condition or disease in a mammal comprising administering to said mammal a pharmaceutical composition as defined in claim **48**.

50. A method of screening for an agent that inhibits the catalytic activity of PTPbr7, comprising the steps of: exposing a cell line expressing PTPbr7 and capable of responding to NGF, to an amount of NGF, in the presence and absence of a test agent, under conditions suitable for detectable neurite growth to occur in the presence of a PTPbr7 inhibitor, detecting said neurite growth, and comparing said neurite growth, where a PTPbr7 inhibitor is a test agent whose presence results in more neurite growth than its absence.

51. The method as defined in claim **50** wherein said cell line is a PC12 cell line, or a PC12 cell line transfected with a PTPbr7.

52. The method as defined in claim **51** wherein said transfected PC12 cell line overexpresses said PTPbr7.